

(FILE 'HOME' ENTERED AT 11:52:16 ON 26 NOV 2002)

FILE 'REGISTRY' ENTERED AT 11:52:33 ON 26 NOV 2002

L1           STRUCTURE UPLOADED  
L2           2 S L1 SSS SAM  
L3           17 S L1 SSS FULL

FILE 'CAPLUS' ENTERED AT 11:53:22 ON 26 NOV 2002

L4           7 S L3  
L5           5 S L4 AND (DNA OR RNA OR NUCLEIC ACID)

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:850353 CAPLUS  
TITLE: Nucleic acid labeling compounds of heterocyclic derivatives containing a detectable moiety  
INVENTOR(S): McGall, Glenn; Barone, Anthony D.  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S. Pat. Appl. Publ., 68 pp., Cont.-in-part of U. S. 6,344,316.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002165372	A1	20021107	US 2001-952387	20010911
WO 9727317	A1	19970731	WO 1997-US1603	19970122
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6344316	B1	20020205	US 1997-882649	19970625
PRIORITY APPLN. INFO.:				
			US 1996-10471P	P 19960123
			US 1997-35170P	P 19970109
			WO 1997-US1603	A1 19970122
			US 1997-882649	A2 19970625
			US 2000-231827P	P 20000911

AB The invention concerns nucleic acid labeling compds. contg. heterocyclic derivs. The heterocyclic deriv. contg. compds. are synthesized by condensing a heterocyclic deriv. with a cyclic group (e.g. a ribofuranose deriv.). The labeling compds. are suitable for enzymic attachment to a nucleic acid, either terminally or internally, to provide a mechanism of nucleic acid detection.

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:716440 CAPLUS  
DOCUMENT NUMBER: 137:227613  
TITLE: Nucleic acid labeling compounds  
INVENTOR(S): McGall, Glenn; Barone, Anthony D.  
PATENT ASSIGNEE(S): Affymetrix, Inc., USA  
SOURCE: PCT Int. Appl., 63 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002072779	A2	20020919	WO 2002-US7584	20020312
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,				

BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
PRIORITY APPLN. INFO.: US 2001-275202P P 20010312  
OTHER SOURCE(S): MARPAT 137:227613

AB The present invention relates to nucleic acid labeling compds. More specifically, the invention provides compds. contg. a detectable moiety. The invention also provides methods of making these compds. It further provides methods of attaching the compds. to a nucleic acid. The nucleic acid labeling compds. or the present invention are effectively incorporated into a nucleic acids to provide readily detectable compns. that are useful for genetic anal. technologies. These compds. and the detectable compns. can aid, for example, in the monitoring of gene expression and the detection and screening of mutations and polymorphisms. Thus, the compds. of the invention are suitable for enzymic incorporation into nucleic acids. Furthermore, the nucleic acids to which the labeling compd. are attached maintain their ability to bind to a probe, such as, for example a complementary nucleic acid. The present invention provides nucleic acid labeling compds. that are capable of being enzymically incorporated into a nucleic acid. The nucleic acids to which the compds. are attached maintain their ability to bind to a complementary nucleic acid sequence. The compds. are synthesized by condensing a heterocyclic deriv. with a cyclic group (e.g. a ribofuranose deriv.).

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:608932 CAPLUS

DOCUMENT NUMBER: 133:190215

TITLE: Methods for making morpholino-nucleotides, and their use for analyzing and marking nucleic acid sequences

INVENTOR(S): Marciacq, Florence; Sauvaigo, Sylvie; Mouret, Jean-Francois; Issartel, Jean-Paul; Molko, Didier

PATENT ASSIGNEE(S): Commissariat A L'Energie Atomique, Fr.; Centre National De La Recherche Scientifique

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050626	A1	20000831	WO 2000-FR427	20000221
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
FR 2790004	A1	20000825	FR 1999-2170	19990222
FR 2790005	A1	20000825	FR 1999-12001	19990927
EP 1155140	A1	20011121	EP 2000-906441	20000221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

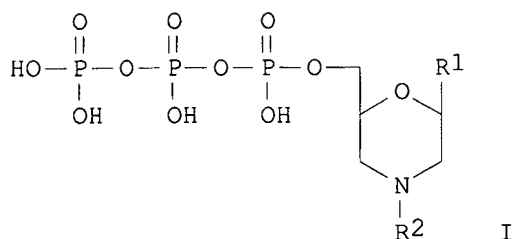
PRIORITY APPLN. INFO.: FR 1999-2170 A 19990222

FR 1999-12001 A 19990927

WO 2000-FR427 W 20000221

OTHER SOURCE(S): CASREACT 133:190215; MARPAT 133:190215

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AB The invention concerns the use of morpholino-nucleosides of formula (I) wherein: R1 represents a nucleic base and R2 represents a group corresponding to the following formulas:  $-(CH_2)_n-NH_2$ ,  $-(CH_2)_n-SH$ ,  $-(CH_2)_n-COOH$ ,  $-(CH_2)_n-OH$ ,  $-(CH_2)_n-NH-R_3$ ,  $(CH_2)_n-SR_3-(CH_2)_n-CO-R_3$ ,  $-(CH_2)_n-OR_3$  wherein: n is an integer ranging from 1 to 12 and R3 is a group derived from a marker, a protein, an enzyme, a fatty acid or a peptide, as chain terminators in a DNA or RNA sequencing process by Sanger method, or for marking DNA or RNA fragments.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:122205 CAPLUS

DOCUMENT NUMBER: 132:293960

TITLE: Synthesis, Biological Activity, and Molecular Modeling of Ribose-Modified Deoxyadenosine Bisphosphate Analogues as P2Y1 Receptor Ligands

AUTHOR(S): Nandanan, Erathodiyil; Jang, Soo-Yeon; Moro, Stefano; Kim, Hea Ok; Siddiqui, Maqbool A.; Russ, Pamela; Marquez, Victor E.; Busson, Roger; Herdewijn, Piet; Harden, T. Kendall; Boyer, Jose L.; Jacobson, Kenneth A.

CORPORATE SOURCE: Molecular Recognition Section Laboratory of Bioorganic Chemistry National Institute of Diabetes Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD, 20892-0810, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(5), 829-842  
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The structure-activity relationships of adenosine-3',5'-bisphosphates as P2Y1 receptor antagonists have been explored, revealing the potency-enhancing effects of the N6-Me group and the ability to substitute the ribose moiety (Nandanan et al. J. Med. Chem. 1999, 42, 1625-1638). The authors have introduced constrained carbocyclic rings (to explore the role of sugar puckering), non-glycosyl bonds to the adenine moiety, and a phosphate group shift. The biol. activity of each analog at P2Y1 receptors was characterized by measuring its capacity to stimulate phospholipase C in turkey erythrocyte membranes (agonist effect) and to inhibit its stimulation elicited by 30 nM 2-methylthioadenosine-5'-diphosphate (antagonist effect). Addn. of the N6-Me group in several cases converted pure agonists to antagonists. A carbocyclic N6-methyl-2'-deoxyadenosine bisphosphate analog was a pure P2Y1 receptor antagonist and equipotent to the ribose analog (MRS 2179). In the series of ring-constrained methanocarba derivs. where a fused cyclopropane moiety constrained the pseudosugar ring of the nucleoside to either a Northern (N) or Southern (S) conformation, as defined in the pseudorotational cycle, the 6-NH2 (N)-analog was a pure agonist of EC50 155 nM and 86-fold more potent than the corresponding (S)-isomer. The 2-chloro-N6-methyl-(N)-methanocarba analog was an antagonist of IC50 51.6 nM; thus, the ribose ring (N)-conformation appeared to be favored in recognition at P2Y1

receptors. A cyclobutyl analog was an antagonist with IC50 of 805 nM, while morpholine ring-contg. analogs were nearly inactive. Anhydrohexitol ring-modified bisphosphate derivs. displayed micromolar potency as agonists (6-NH2) or antagonists (N6-methyl). A mol. model of the energy-minimized structures of the potent antagonists suggested that the two phosphate groups may occupy common regions. The (N)- and (S)-methanocarba agonist analogs were docked into the putative binding site of the previously reported P2Y1 receptor model.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:380243 CAPLUS

DOCUMENT NUMBER: 131:73915

TITLE: Synthesis and enzymatic incorporation of morpholino thymidine-5'-triphosphate in DNA fragments

AUTHOR(S): Marciacq, Florence; Sauvaigo, Sylvie; Issartel, Jean-Paul; Mouret, Jean-Francois; Molko, Didier

CORPORATE SOURCE: Departement de Recherche Fondamentale sur la Matiere Condensee - Service de Chimie Inorganique and Biologique Laboratoire des Lesions des Acides Nucleiques, Grenoble, 38054, Fr.

SOURCE: Tetrahedron Letters (1999), 40(25), 4673-4676

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 4-(Carboxymethyl)-2-(thymidin-9-yl)-6-(hydroxymethyl)morpholine-6-triphosphate (morpholino thymidine-5'-triphosphate) was synthesized from 1-(.beta.-D-ribo-pentofuranosyl) thymine. It was fully characterized by NMR, UV and mass spectrometry. Taq polymerase enzymic incorporation of this nucleotide analog into DNA fragments was investigated. Morpholino thymidine-5'-triphosphate was incorporated in a base-specific process and acted as a novel chain terminator in DNA sequencing, similarly to the corresponding dideoxynucleotide.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1984:22974 CAPLUS

DOCUMENT NUMBER: 100:22974

TITLE: 2,5-Riboadenylate-morpholinoadenylate nucleotides

INVENTOR(S): Torrence, Paul F.; Imai, Jiru; Johnston, Margaret

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: U. S. Pat. Appl., 44 pp. Avail. NTIS Order No.

PAT-APPL-6-455 727.

CODEN: XAXXAV

DOCUMENT TYPE: Patent

LANGUAGE: English

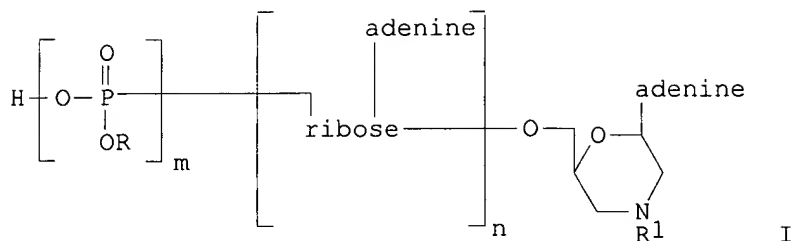
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 468950	A0	19830902	US 1983-468950	19830223
US 4515781	A	19850507		
JP 59205394	A2	19841120	JP 1984-31577	19840223
JP 01053880	B4	19891115		

PRIORITY APPLN. INFO.: US 1983-468950 19830223

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AB The title 2'-5' oligonucleotides I [ $m = 0-4$ ;  $n = 1-15$ ;  $R = H$ , adenosine, alkyl;  $R_1 = H$ , (un)substituted hydrocarbyl], useful for fine tuning in antitumoral chemotherapy and for avoiding interferon-induced auto-immune diseases (biol. data given), were prepd. Thus, 2'-5' (pA)<sub>4</sub> was oxidized with NaIO<sub>4</sub> and then treated with hexylamine and NaBH<sub>3</sub>CN to give 85% I ( $m = 1$ ,  $n = 3$ ,  $R = H$ ,  $R_1 = \text{hexyl}$ ).

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:3394 CAPLUS

DOCUMENT NUMBER: 98:3394

TITLE: Chemical modification potentiates the biological activities of 2-5A and its congeners

AUTHOR(S): Imai, Jiro; Johnston, Margaret I.; Torrence, Paul F.

CORPORATE SOURCE: Lab. Chem., Natl. Inst. Arthritis, Diabetes, Dig. Kidney Dis., Bethesda, MD, 20205, USA

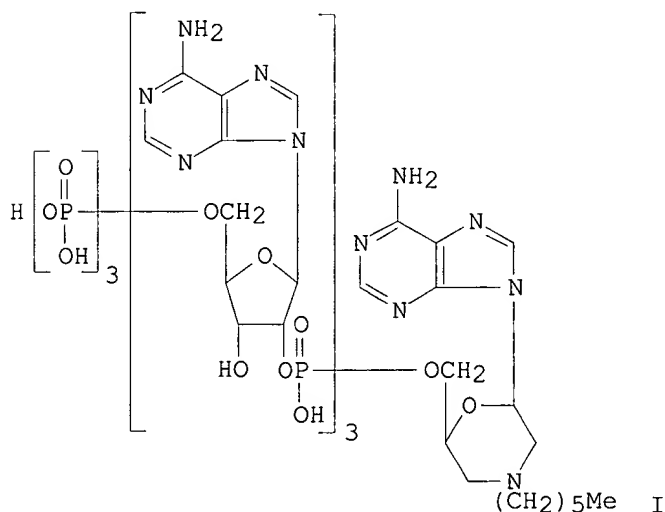
SOURCE: Journal of Biological Chemistry (1982), 257(21), 12739-45

CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: Journal

LANGUAGE: English

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AB Chem. modification of p5'A2'(p5'A2')np5'A (oligoadenylates) by a periodate oxidn./Schiff base formation/borohydride redn. cycle gave a series of oligoadenylate analogs in which the ribose of the 2'-terminal nucleotide was transformed to an N-substituted morpholine (azahexapyranose). 2',5'-Oligoriboadenylated 5'-monophosphates bearing this modifications were 5-10-fold more potent as antagonists of the action of

ppp5'A2'p5'A2'p5'A2'p5'A (i.e. the unmodified tetramer triphosphate) or poly(I).cntdot.poly(C) than was unmodified p5'A2'p5'A2'p5'A (i.e. the unmodified tetramer monophosphate). Application of this modification to the tetramer triphosphate ppp5'A2'p5'A2'p5'A2'p5'A resulted in an analog (I) with 10-fold the activity of ppp5'A2'p5'A2'p5'A (i.e. the unmodified trimer triphosphate) as an inhibitor of protein synthesis or activator of the 2'.fwdarw.5'-oligoadenylate-dependent endoribonuclease. This new analog, the most potent oligoadenylate deriv. reported to date, inhibited translation in exts. of mouse L-cells programmed with encephalomyocarditis virus RNA at a concn. of 10<sup>-10</sup> M (concn. for half-maximal inhibition). All such N-substituted morpholine modified 2'.fwdarw.5'-oligoadenylates were extremely resistant to degrdn. by L-cell exts. under conditions where unmodified 2'.fwdarw.5'-oligoadenylates were quickly destroyed. These data demonstrated the necessity for an intact terminal ribose ring for the action of the 2'.fwdarw.5'-oligoadenylate phosphodiesterase. Thus, extensive chem. modification of the 2' terminus of 2'.fwdarw.5'-oligoadenylate may be possible without adversely affecting its biol. activity while endowing it with other favorable properties such as resistance to degrdn.

=>

**SEARCH REQUEST FORM****Scientific and Technical Information Center**

Requester's Full Name: Patrick Lewis Examiner #: 79002 Date: 11-26-02  
 Art Unit: 1623 Phone Number 305-4043 Serial Number: 09/914,221  
 Mail Box and Bldg/Room Location: CM/8012 Results Format Preferred (circle): PAPER DISK E-MAIL  
CM/8019

**If more than one search is submitted, please prioritize searches in order of need.**

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

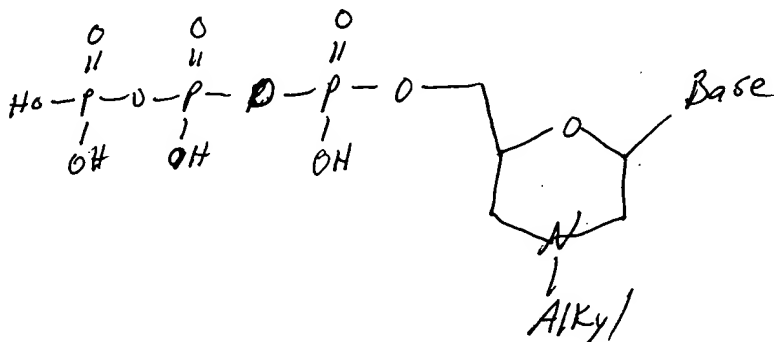
Title of Invention: Method of making morpholino-nucleotides, and their use for...

Inventors (please provide full names): Florence Marciacq, Sylvie Sauvageo, Jean-Francois Meuret, Didier Molko

Earliest Priority Filing Date: 1-22-99

*\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

- Process for manufacturing a 3'-labeled nucleic acid via enzymatic incorporation of:



see claim 1